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Cardiovascular disease prevention and management in COVID-19: a clinical consensus statement of the European Association of Preventive Cardiology, the European Association of Cardiovascular Imaging, the Association of Cardiovascular Nursing & Allied Professions, the European Association of Percutaneous Cardiovascular Interventions, and the Heart Failure Association of the ESC

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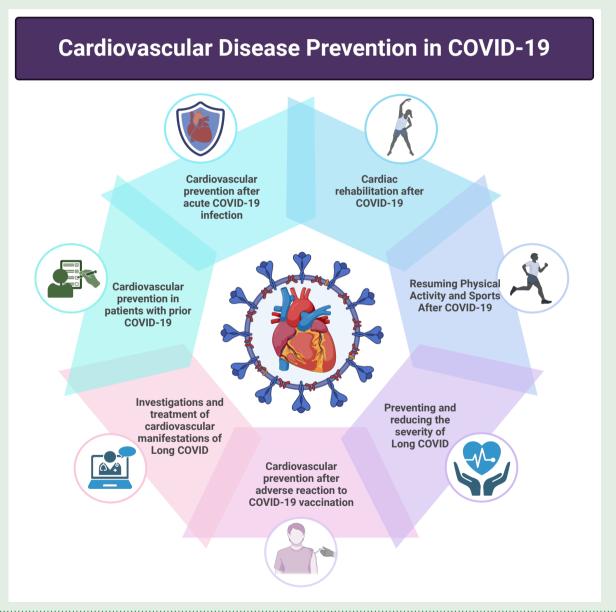
#### **Abstract**

The coronavirus-associated disease 2019 (COVID-19) pandemic has posed significant challenges due to the complex interplay between SARS-CoV-2 infection and cardiovascular disease. COVID-19 can trigger and exacerbate cardiovascular complications, observed both during the acute phase of infection and in the post-acute phase, with some individuals developing long-term sequelae collectively termed Long COVID. Additionally, reinfection and adverse reactions to COVID-19 vaccines may contribute to cardiovascular events. This clinical consensus statement, developed by associations of the European

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Society of Cardiology, aims to provide a comprehensive overview of cardiovascular prevention strategies across all stages of COVID-19. These include addressing cardiovascular risk associated with acute infection, prior infection, Long COVID, reinfection, and post-vaccination events. Key recommendations focus on preventing and managing cardiovascular manifestations in patients with acute or prior COVID-19, implementing targeted cardiovascular rehabilitation, and introducing interventions to mitigate the severity of Long COVID. The document also emphasizes lifestyle modifications and personalized therapeutic approaches to enhance patient outcomes. Given the evolving nature of COVID-19 and its long-term cardiovascular implications, ongoing research is crucial to address existing knowledge gaps, optimize preventive strategies, and improve patient care. Future studies should prioritize the individualization of preventive measures for diverse populations, refine rehabilitation strategies, and advance long-term cardiovascular care, ensuring that evidence-based practices continue to evolve alongside emerging data.

### **Graphical Abstract**



### Introduction

Coronavirus disease 2019 (COVID-19), caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), continues to exert a profound impact on global morbidity and mortality. To date, over 10 million deaths and nearly 1 billion documented cases have been reported worldwide, although these figures likely underestimate the true scale of the pandemic. Cardiovascular complications represent a common pathway of SARS-CoV-2 pathophysiology. Treatments such as corticosteroids, which have demonstrated clear benefits during the acute phase of infection in hospitalized patients, are known to adversely affect cardiac physiology, potentially leading to unfavourable short- and long-term outcomes. This holds true regardless of vaccination status, although vaccines have been instrumental in significantly reducing the burden of morbidity and mortality during both acute and post-acute phases of infection.

Emerging evidence highlights the prevalence of cardiovascular complications not only during the acute phase but also in the longer term, referred to as Long COVID, Post-COVID Condition, Post-COVID Syndrome, or Post-COVID Sequelae.<sup>4</sup> The World Health Organization (WHO) defines Long COVID as the onset of new symptoms within 3 months of an acute COVID-19 infection, persisting for over 2 months with no alternative explanation.<sup>5</sup> While Long COVID encompasses cardiovascular and non-cardiovascular manifestations, this document specifically focuses on the cardiovascular subset, referred to as Cardiac Long COVID.

In the acute phase, cardiovascular complications may include inflammatory conditions such as myocarditis and pericarditis and thrombotic events such as acute myocardial infarction, stroke, deep vein thrombosis and pulmonary embolism, vasospasm, arrhythmias, and heart failure. These complications can persist for months to years, posing diagnostic and management challenges. Symptoms and signs of Cardiac Long COVID include angina, breathlessness, arrhythmias, heart failure, autonomic dysfunction, fatigue, and dizziness, <sup>7–9</sup> many of which are non-specific and can occur independently of SARS-CoV-2 infection, complicating accurate diagnosis. It is estimated that >20% of Long COVID patients experience cardiac symptoms, <sup>3,4</sup> suggesting that potentially 2–5% of all individuals infected with COVID-19 may develop Cardiac Long COVID.

In the absence of evidence-based guidance, patients often seek unproven treatments, which can lead to harm from invasive interventions or adverse effects. Furthermore, pre-existing or newly developed cardiovascular risk factors and comorbidities frequently exacerbate the severity of COVID-19, underlining the urgent need for tailored, comprehensive cardiovascular prevention strategies for patients at risk, with recent or prior infection.

In response to these challenges, this consensus statement from the affiliated associations of the European Society of Cardiology (ESC) seeks to provide comprehensive guidance on cardiovascular prevention across the continuum of COVID-19. By addressing key aspects of managing cardiovascular risk following COVID-19, this document aims to equip clinicians with a practical tool to optimize cardiovascular outcomes for COVID-19 patients.

Objectives of this clinical consensus statement

- To identify and establish consensus on preventive measures that reduce the risk of long-term cardiovascular complications following COVID-19
- (2) To promote interventions to reduce the incidence and severity of Cardiac Long COVID

- (3) To define the indications and role of cardiac rehabilitation following COVID-19 infection
- (4) To highlight established strategies for cardiovascular prevention after adverse events related to vaccination
- (5) To identify areas where further research could be considered.

### **Methods**

We previously published a systematic review synthesizing the evidence available on Cardiac Long COVID until July 2023, which served as the foundation reference for this consensus statement.

Additionally, key articles published after that review were incorporated. Following the completion of the manuscript and the associated clinical implications, an online Delphi exercise was conducted to identify agreement. All clinical implication statements have been supported by >90% of the coauthors (see Supplementary material online, material). The co-authors collaboratively drafted the manuscript, and all approved the final text.

# Cardiovascular prevention after acute COVID-19 infection

Following an acute SARS-CoV-2 infection, cardiovascular risk factors such as inflammation, <sup>10</sup> endothelial dysfunction, <sup>11</sup> and thrombosis <sup>12</sup> are significantly elevated. <sup>13</sup> These pathophysiological mechanisms can in a minority of infected patients contribute to cardiac complications, including myocarditis, myocardial infarction, heart failure, and arterial or venous thromboembolism, affecting both previously healthy individuals and, to a greater extent, those with pre-existing cardiovascular disease (CVD). <sup>14,15</sup> Early and proactive cardiovascular prevention is essential to mitigate these risks and improve clinical outcomes <sup>16</sup> in all patients but especially those with elevated markers of cardiac injury such as troponin or NTProBNP.

As the initial public health messaging largely focused on pulmonary complications of COVID 19, many people with COVID-19 may not be aware of the increased cardiovascular risks associated to the disease. As CVD symptoms can emerge weeks or even years after the acute infection, preventive strategies should begin with early patient education. This includes discussions on potential symptoms associated with slowly progressing and severe conditions, such as myocarditis, heart failure, and thrombosis, to enable patients to recognize and report these symptoms promptly. Lifestyle interventions, including promoting regular physical activity, smoking cessation, blood pressure optimization, glycaemic control, <sup>17</sup> and dietary modifications, should also be prioritized as part of comprehensive risk reduction strategies. <sup>18</sup> Obesity can be managed with lifestyle interventions and pharmacotherapy as detailed in the recent ESC consensus statement on obesity and CVD. <sup>19</sup>

Additionally, vaccination has demonstrated a protective role against Long COVID and COVID-19-related CVD<sup>3,20</sup> and is more extensively discussed in the 'Preventing and reducing the severity of Long COVID' section of this statement.

The use of prophylactic aspirin or anticoagulation without a specific clinical indication is not currently advised, as evidence to support this approach is lacking, and the associated risk of bleeding complications is not negligible. Furthermore, while Cardiac Long COVID-specific risk scores have been developed, 22 their predictive utility at the individual level remains unclear, and routine use of these scores is not presently advised, although this remains an area of research potential.

Clinical advice

- Early patient education post-acute COVID-19 infection on potential symptoms of Cardiac Long COVID can empower individuals to report relevant symptoms early on.
- Awareness and prompt management of modifiable risk factors, including hypertension, hyperlipidaemia, hyperglycaemia, smoking cessation, and lifestyle modifications promoting healthy nutrition and physical activity, is crucial.

- Vaccination and booster doses should be encouraged in patients who are unvaccinated or have not received the recommended boosters, particularly if they belong to high-risk groups, as they may reduce both the risk of Long COVID and COVID-19 related cardiovascular complications.
- Current evidence does not support the routine use of antiplatelets or anticoagulants following acute COVID-19 infection to prevent cardiovascular complications or mitigate cardiac Long COVID risks.

#### Cardiac rehabilitation after COVID-19

Cardiac rehabilitation following SARS-CoV-2 infection is a critical component of the recovery process, particularly for patients who have experienced cardiovascular complications such as myocardial infarction, myocarditis, thrombosis, or heart failure. <sup>23</sup> It is also essential for those reporting chronic fatigue at rest or exercise intolerance during low physical activity levels. In such cases, rehabilitation aims to restore cardiopulmonary function and improve exercise capacity through a structured programme incorporating exercise, education, lifestyle interventions (e.g. healthy nutrition <sup>24</sup> and smoking cessation <sup>17,25</sup>) and optimal pharmacological management. <sup>26</sup> Generating awareness of the importance of cardiac rehabilitation both in patients and healthcare professionals and early implementation of rehabilitation can help mitigate long-term sequelae and improve overall cardiovascular outcomes.

Rehabilitation programmes should be tailored to address key symptoms, including dyspnoea<sup>27</sup> on exertion, atypical angina, palpitations, general fatigue, and orthostatic intolerance (OI), where sometimes energy conservation may be appropriate, while accounting for individual needs, the severity of COVID-19, psychological aspects (including anxiety, depression, and other mental health conditions, <sup>28</sup> which could play a role in symptomatology), and pre-existing cardiovascular or cardiopulmonary conditions. 29 Exercise training should be guided by cardiopulmonary exercise testing, particularly by assessing ventilatory thresholds to prescribe appropriate exercise intensities. Pulmonary function and diffusion capacity should also be evaluated to identify any significant post-COVID-19 pulmonary involvement. Rehabilitation programmes also offer a valuable opportunity for holistic patient assessment and the implementation of the preventive strategies outlined in this statement. Equitable access to these programmes should be prioritized, particularly for individuals from rural or socioeconomically disadvantaged backgrounds, who remain underrepresented in rehabilitation services.

A multidisciplinary approach involving cardiologists, physiotherapists, psychologists, nurses and allied health professionals, and primary care providers is crucial in establishing a comprehensive recovery plan.<sup>23</sup> The rehabilitation process should focus on gradual physical reconditioning, psychological support, and adherence to pharmacological therapies. Post-COVID-19 patients often present with severe impairment in maximal and aerobic exercise capacity. Therefore, exercise should commence at low intensity (e.g. 25 W) for short durations (e.g. 5 min), with gradual increases in intensity and duration over 6-12 weeks. Isometric resistance exercises, such as wall sits, may be initiated early, while machine-based exercises can be introduced later, contingent on the patient's tolerance to endurance activities. This stepwise approach aims to manage post-exercise fatigue and prevent early discontinuation. A sample of this stepwise approach can be seen in Figure 1. Adjustments to rehabilitation intensity should be made according to the patient's progress and any signs of cardiovascular distress.<sup>23</sup> Regular follow-up and cardiopulmonary monitoring are vital to detect persistent or emerging symptoms and to track progress with fatigue and other cardiopulmonary issues.

The overarching goal of cardiac rehabilitation post-COVID is to enhance quality of life, facilitate an earlier return to work where appropriate, and reduce the risk of future cardiovascular events including mortality, coronary syndromes, strokes, and venous thromboembolism. The integration of technology and artificial intelligence can further enhance patient and clinician engagement. Smart devices, such as smartwatches paired with smartphone applications, enable real-time tracking of daily activity and health metrics (e.g. heart rate, sleep duration, and heart rate variability). These tools provide objective data on physical activity and recovery trends, aiding

in achieving predefined targets.  $^{31}$  Virtual consultations can be convenient, but face-to-face sessions may increase adherence when combined with virtual ones.  $^{32}$ 

#### Clinical advice

- Cardiac rehabilitation is advised for all patients with cardiovascular complications post-COVID to restore physical and mental health and improve functional capacity. This should focus on structured exercise, nutritional advice, and psychological support.
- To optimize recovery, multidisciplinary care, including regular monitoring, is advised during cardiac rehabilitation post-COVID.
- Tailored exercise programmes are advised to facilitate a gradual and appropriate improvement in exercise capacity. Impact of frequency, type, and intensity of exercise (typically prescribed as a percentage of heart rate reserve or rate of perceived exertion) is uncertain in the early phase after COVID-19, in patients with impaired exercise capacity or cardiopulmonary symptoms. Low or very low exercise intensity at short duration may be appropriate at the beginning.
- Regular cardiopulmonary monitoring is crucial during the rehabilitation phase to ensure safe and effective progress, which may be aided by technology and telemedicine.
- While many aspects of cardiac rehabilitation can be achieved remotely, face-to-face sessions complementing virtual sessions may improve adherence.
- Access to cardiac rehabilitation for Long COVID patients varies regionally, and its cost-effectiveness has yet to be fully determined.

# Cardiovascular prevention in patients with prior COVID-19

Patients who have recovered from acute COVID-19 remain at more than twice the risk of cardiovascular events than the general population. This is likely due to persistent inflammation, endothelial dysfunction, microthrombi, potential myocardial injury, and an increased prevalence of hypertension and Type 2 diabetes mellitus with symptoms and signs manifesting within 3 months from the acute infection. Preventive strategies for this population should prioritize the early identification of residual cardiovascular risk and the long-term management of modifiable factors, including hypertension, diabetes, dyslipidaemia, smoking cessation, physical inactivity, and nutritional optimization. Tr.24 Tailored pharmacological interventions may be particularly beneficial in patients with clinical evidence of heart failure, myocarditis, atrial fibrillation, or thrombosis, aligning with the ESC guidelines for managing these conditions.

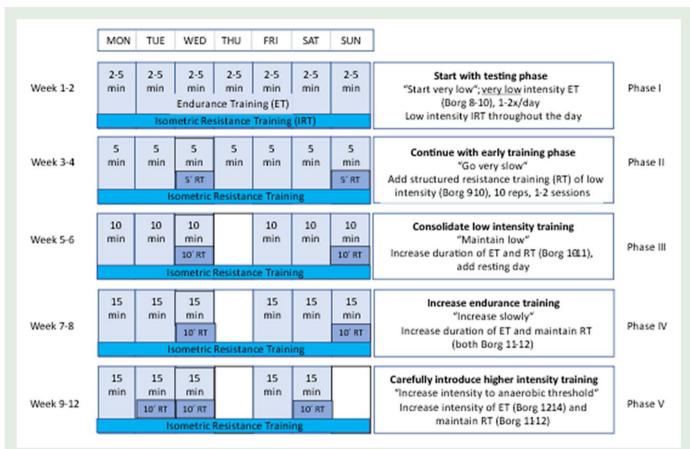
Importantly, patients hospitalized with COVID-19 exhibit an elevated risk of cardiovascular events lasting up to 3 years post-infection.<sup>39</sup> This holds true for both patients with mild acute COVID-19 who have a two-fold risk, but also those with severe infection requiring hospitalization who have an almost four-fold risk. Early engagement in a multidisciplinary care setting, including patient education and cardiac rehabilitation programmes, may help mitigate the risk of future cardiac events.<sup>40</sup>

#### Clinical advice

- History of COVID-19 infection is associated with a higher risk of incident cardiovascular events in some individuals.
- Early identification and proactive management of risk factors may be important in preventing cardiovascular complications due to Long COVID.
- Comprehensive prevention strategies should incorporate pharmacological and lifestyle interventions to address residual cardiovascular risks.

# Investigations and treatment of cardiovascular manifestations of Long COVID

Long COVID is characterized by persistent cardiovascular symptoms, including chest pain, palpitations, shortness of breath, and OI, which may persist for months following acute infection. <sup>41</sup> These symptoms can occur even in individuals without pre-existing heart conditions, highlighting the significant cardiovascular impact of this condition.



**Figure 1** Exercise training schedule for patients with Long COVID (exercise training Phases I–V). Key components are a very low intensity introductory or testing Phase I, which is followed by a Phase II of maintaining very low intensity. Isometric exercises, e.g. wall sits, are introduced from the beginning and continuously increased in time according to the patient's subjective conditions. Phases III–V will gradually increase duration and intensity, and any side effects of training, e.g. fatigue or muscle pain, will be monitored continuously. This will influence mode, frequency, duration, and intensity of exercise training. The general principle is to avoid starting with moderate to higher intensity as with other training schedules for sedentary individuals. If symptoms occur, then the training of the next lower phase should be continued.

Cardiac function is regulated through complex interactions between cardiomyocytes, fibroblasts, endothelial cells, and cytokines. Cardiomyocytes facilitate cardiac contraction, fibroblasts provide structural support and aid in tissue repair, while cytokines mediate immune responses and inflammation. During periods of cardiac stress or injury, such as during acute SARS-CoV-2 infection, this balance is disrupted, leading to abnormal signal-ling, persistent inflammation, adverse remodelling, and symptoms indicative of heart failure. This section explores the potential mechanisms underlying these symptoms and outlines a stepwise approach to their investigation to facilitate accurate diagnosis, recognizing that some cases may involve underlying organic pathology requiring targeted therapy.

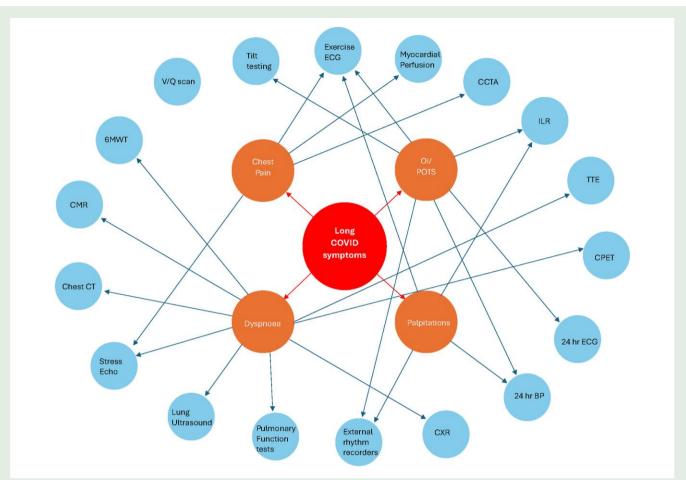
Emerging studies in COVID-19 survivors indicate an increased risk of cardiovascular events, including HF, ischaemic and non-ischaemic cardiomyopathy, cardiac arrest, and cardiogenic shock. <sup>6,7</sup> This risk is most pronounced in the early period following acute infection but may persist to varying degrees, even among vaccinated individuals. <sup>6,45</sup> Between 3 and 9 months post-hospitalization, these patients also face elevated risks of emergency department visits or hospitalizations for conditions such as diabetes, hypertension, and HF compared with COVID-19-naïve individuals. <sup>46</sup> Patients with angina as part of Cardiac Long COVID also have a high prevalence of myocardial ischaemia with no coronary obstruction, largely related to derangement of the endothelium-dependent pathway. <sup>47</sup> Diagnosing new-onset HF in these patients require adherence to established guidelines, as symptoms of Long COVID, including persistent dyspnoea, fatigue, chest pain, and palpitations, may overlap with HF presentations. Comprehensive

evaluation, incorporating physical examination, multimodality cardiac imaging, and laboratory testing, is essential for identifying at-risk patients and summarized in *Figure 2* and *Supplementary material online*, *Table S1* (imaging modalities in Long COVID evaluation and potential findings) and *Table 1* (imaging modalities tailored to symptomatology). Measurement of brain natriuretic peptide levels should be routine in patients presenting with symptoms suggestive of new or worsening HF, as these biomarkers can assist in the early diagnosis or exclusion of HF.

#### Management of cardiovascular manifestations

The treatment of cardiovascular complications in Long COVID necessitates a multidisciplinary approach, prioritizing symptom management, risk stratification, and targeted interventions. Initial concerns regarding the use of angiotensin converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARBs) in chronic HF management during the pandemic stemmed from their potential to upregulate Angiotensin-2 receptors, potentially exacerbating outcomes. However, subsequent studies 48,49 demonstrated no increase in all-cause mortality associated with the long-term use of ACEi/ARBs, reaffirming their role in guideline-directed medical therapy for HF.

Current HF management encompasses four primary therapeutic pillars: ACEi, ARB, or angiotensin receptor-neprilysin inhibitors (ARNI) (considered collectively), alongside mineralocorticoid receptor antagonists (MRAs), betablockers, and sodium-glucose cotransporter 2 (SGLT2) inhibitors for patients with reduced, mildly reduced, and preserved left ventricular ejection fraction



**Figure 2** A tree diagram highlighting non-invasive tests in patients presenting with symptoms or conditions that could be attributed to Long COVID. 6MWT, 6 min walk test; BP, blood pressure; CPET, cardiopulmonary exercise test; CMR, cardiovascular magnetic resonance; CT, computed tomography; ECG, electrocardiography; h, hour; ILR, implantable loop recorder; OI, orthostatic intolerance; POTS, postural orthostatic tachycardia syndrome.

(LVEF). These therapies should be administered according to guideline recommendations, 34,35 including patients with a history of COVID-19, with treatment individualized based on HF subtype and patient symptomatology. For patients experiencing recurrent arrhythmias, including inappropriate sinus tachycardia, antiarrhythmic therapy, such as beta-blockers or as a second-line ivabradine, may be warranted and are generally well tolerated. 50 For patients with myocardial ischaemia of non-obstructive origin diagnosed with intracoronary functional testing (acetylcholine test and coronary flow reserve/microvascular resistance measurements), stratified treatment as recommended in the ESC guidelines on management of chronic coronary syndromes<sup>37</sup> can improve angina frequency and stability. <sup>47</sup> Similarly, anticoagulation therapy may be indicated for hospitalized patients following discharge in those at high risk of thromboembolism (such as those with modified IMPROVE VTE score of at least 4) with evidence only based on observational data. 51,52 Continuous monitoring through imaging and biomarker assessments is critical for tailoring and optimizing therapy.

#### Orthostatic intolerance and autonomic dysregulation

OI, including orthostatic hypotension and postural orthostatic tachycardia syndrome (POTS), frequently affects Long COVID patients, more so women, <sup>53</sup> often resulting from hypovolaemia or deconditioning due to prolonged bed rest. <sup>54–56</sup> Dysregulation of the autonomic nervous system, characterized by abnormal epinephrine and norepinephrine levels, exacerbates these symptoms, with contributing factors including venous pooling,

volume dysregulation, autoimmunity, and a hyperadrenergic state. <sup>57,58</sup> SARS-CoV-2 infection-induced RAAS imbalance and sympathetic nervous system damage may further drive the development of dysautonomia and POTS. <sup>59</sup> Common POTS symptoms such as nausea, dizziness, fatigue, and cognitive impairment significantly reduce quality of life and exercise tolerance, often linked to muscle wasting and reduced endurance post-COVID-19. <sup>60</sup> Management includes avoidance of any trigger factors such as prolonged standing or excessive heat, lifestyle modifications (including adequate water and salt intake), use of compression stockings, and if symptoms persist, pharmacological treatment could be advised including fludrocortisone, midodrine, or even beta-blockers and ivabradine for some patients. <sup>50,61</sup>

#### Preventive measures

Management strategies for Long COVID patients should include personalized rehabilitation programmes as discussed in the rehabilitation section of this statement. <sup>26</sup> Screening high-risk individuals, such as hospitalized patients, is essential for detecting conditions like myocarditis, HF, and arrhythmias, which may benefit from targeted treatment. Close follow-up and personalized care plans are integral to addressing the diverse cardiovascular manifestations of Long COVID effectively.

Clinical advice

• Symptom-based diagnostic approaches are crucial, as summarized in *Figure 2* and *Table 1*.

Clinical scenario	Initial diagnostic test(s) based on cardiac or pulmonary origin of the symptom	Follow-up non-invasive tests	Additional considerations
Dyspnoea with suspected lung pathology	Spirometry and chest X-ray	If abnormal:  Chest CT (especially when chest radiography abnormal)  MWT  CPET (if available)	Electrocardiogram (ECG) is advised a first test as well, due to possibility of associated cardiovascular diseases and its wide availability Considering patient profile, additional risk factors or previous pathologies, other examinations may be necessary, e.g. PHT evaluation with the necessity of V/Q scan
Dyspnoea with normal spirometry—HF probability	ECG ± chest X-ray	<ul> <li>If ECG abnormal or inconclusive:</li> <li>Transthoracic echocardiography (TTE)</li> <li>Cardiac magnetic resonance imaging (CMR) for myocardial tissue characterization</li> </ul>	A normal ECG does not exclude cardiac pathology.  HF probability detection using the available guidelines and probability scores; completed by CPET combined or not with stress echocardiography and lung ultrasound
Dyspnoea or chest pain with suspicion of ischaemia	ECG Baseline TTE	Ischaemic heart disease pre-test clinical likelihood based on 2024 ESC Guidelines on Chronic Coronary Syndromes <sup>37</sup> • ECG-gated CCTA  • Stress echocardiography or or  • Myocardial perfusion with: single photon emission computer tomography, positron emission tomography-computed tomography or CMR  • Exercise ECG (only if other functional methods unavailable)	Choice of method depends on clinical likelihood and local availability. If available, it is advised to undertake non-radiation investigations first
Palpitations without other symptoms	ECG 24 h ECG monitoring 7–15 day monitoring with use of patches	Intracoronary functional testing     Additional TTE evaluation	Evaluate frequency and duration of symptoms to select the appropriate diagnostic approach.  External or implantable loop recorders (ILRs) is symptoms are persistent but infrequent and the possibility of a negative 24 h monitoring
Symptoms compatible with OI (e.g. brain fog, dizziness, and syncope)	Hypotension orthostatic testing ECG	<ul> <li>Tilt testing</li> <li>24 h ECG monitoring</li> <li>External or implantable ILRs</li> <li>24 h ambulatory blood pressure (BP) monitoring</li> </ul>	Comprehensive evaluation is advised to identify underlying autonomic dysfunction or cardiovascular causes

6MWT, 6 min walk test; BP, blood pressure; CPET, cardiopulmonary exercise test; CMR, cardiovascular magnetic resonance; CT, computed tomography; ECG, electrocardiography; h, hour; ILR, implantable loop recorder; OI, orthostatic intolerance; POTS, postural orthostatic tachycardia syndrome; TTE, transthoracic echocardiogram.

- Cardiovascular symptoms include chest pain, palpitations, shortness of breath, fatigue, arrhythmias, and OI and should prompt consideration of Long COVID.
- Treatment should align with ESC guidelines for heart failure, coronary syndromes, myocardial diseases, and arrhythmias.<sup>34–38</sup>

# Cardiovascular prevention after adverse reaction to COVID-19 vaccination

The well-documented benefits of COVID-19 vaccination in reducing acute severe illness, hospitalizations, and complications are undeniable. However, concerns regarding cardiovascular complications have emerged.

Myocarditis and pericarditis occur at an incidence of 10.7 cases per 100,000, <sup>62</sup> along with reports of arterial and venous thromboembolism, particularly with the AstraZeneca COVID-19 vaccine. <sup>63,64</sup> Additionally, arterial hypertension has been identified in around 3.0% of cases, with serious hypertensive emergencies or Stage III hypertension documented in 0.6%. <sup>65,66</sup> The risks of these complications vary by age and sex <sup>67,68</sup> and do not appear to diminish with repeated vaccinations. <sup>69</sup> Some evidence also suggests that COVID-19 vaccination may be associated with reactivation of latent herpesviruses, <sup>70</sup> which could contribute to cardiovascular complications. However, randomized data evaluating whether herpes zoster vaccination mitigates cardiovascular risk are currently lacking. <sup>71,72</sup>We discuss myocarditis and pericarditis, cardiac risk management post-

vaccination, and medical management of cardiovascular reactions more extensively in the Supplement.

Clinical advice

- Patients should be informed about potential cardiovascular complications and encouraged to seek medical attention promptly if symptoms develop.
- Myocarditis and pericarditis, while rare, are serious adverse reactions to COVID-19 vaccines, with early cardiovascular evaluation and antiinflammatory treatment aiming to prevent long-term sequelae.

Despite the rare risk of adverse events, COVID-19 vaccines significantly reduce the severity of acute illness and Long COVID. As such shared decision-making and further booster vaccination may be of benefit in patients with prior complications, potentially with an alternative vaccine type, especially if deemed at high risk from the acute infection or Long COVID.

# Preventing and reducing the severity of Long COVID

Preventing and mitigating the severity of Long COVID requires early intervention and a comprehensive management approach. <sup>73</sup> Vaccination remains the cornerstone of prevention, significantly reducing the severity of acute COVID-19 and lowering the risk of Long COVID by over 40% in individuals vaccinated with two doses compared with those unvaccinated. For those experiencing persistent symptoms, a multidisciplinary approach is essential to manage and minimize the long-term impact. <sup>26</sup>

#### Early identification and monitoring

Timely identification of high-risk individuals, particularly those with preexisting conditions such as CVD, obesity, and diabetes, is critical to facilitate early intervention and potentially reduce the severity of Long COVID. Applications of Covid C

#### Pharmacological and personalized management

No pharmacological treatments have been demonstrated to alter the disease course of Long COVID. Theoretically pharmacological therapies targeting inflammation, endothelial dysfunction, and thrombosis may help reduce the severity of Long COVID<sup>76</sup>; however, robust evidence supporting these approaches remains lacking. <sup>77</sup> Regular follow-up and cardiac rehabilitation programmes as discussed in the 'Cardiac rehabilitation after COVID-19' section are essential for improving the patients' quality of life. <sup>26</sup>

### Risk factors for Long COVID

Several demographic and clinical risk factors have been linked to the incidence and severity of Long COVID. Non-modifiable factors include older age, female sex, <sup>75</sup> hospitalization during acute COVID-19, and pre-existing comorbidities such as asthma, chronic obstructive pulmonary disease, anxiety or depression, hypertension, diabetes, and ischaemic heart disease. Awareness of these non-modifiable factors allows for early identification and closer monitoring of higher-risk patients, potentially enabling earlier intervention.

Modifiable risk factors include high BMI and smoking, both of which are associated with an increased risk of Long COVID.<sup>3</sup> Weight loss among overweight or obese individuals and smoking cessation may potentially reduce the risk and severity of Long COVID, though prospective studies confirming this are again lacking. Vaccination remains the only proven preventive measure, with a large meta-analysis demonstrating a 43% reduction in Long COVID incidence.<sup>3</sup> Additionally, while evidence is lacking, vaccination in previously unvaccinated individuals suffering from Long COVID may represent a reasonable intervention to reduce symptom duration and severity.

#### Role of antiviral therapy

Pharmacological treatments during acute COVID-19, particularly antiviral drugs, have shown promise in reducing the severity and duration of Long COVID. Observational studies have reported an association between antiviral use and a 27% reduction in post-acute COVID-19 sequelae compared with supportive care. However, the effect in patients with known cardiac disease was not specifically assessed. A retrospective cohort study comparing vaccinated, non-hospitalized patients treated with nirmatrelvir—ritonavir to a matched cohort not receiving the therapy demonstrated a significant reduction in Long COVID incidence. Randomized trials evaluating antiviral therapies for Long COVID are ongoing (NCT05852873; NCT05595369).

Other pharmacological interventions, including leronlimab, coenzyme Q10, combined L-arginine and vitamin C, and probiotics–prebiotics, or interventional studies such as plasma exchange or hyperbaric oxygen therapy, have not demonstrated efficacy in preventing or mitigating Long COVID<sup>80</sup> and are thus not advised.

Clinical advice

- Vaccination is advised to reduce the risk and severity of Long COVID.
- Vaccination may also be appropriate for previously unvaccinated individuals with Long COVID to potentially reduce symptoms.
- Proactive measures to manage obesity and smoking cessation prior to SARS-CoV-2 infection may help lower the incidence of Long COVID.
- Early identification of individuals at higher risk and multidisciplinary management, including lifestyle support and smoking cessation, can be beneficial to mitigate the syndrome's impact.

# Resuming physical activity and sports after COVID-19

Promoting regular physical activity and sports participation is essential for both competitive athletes and sedentary individuals post-COVID-19. While competitive athletes must undergo evaluation to exclude SARS-CoV-2-related cardiovascular complications for a safe return-to-play (RTP), encouraging physical activity is particularly important for sedentary individuals to enhance recovery and overall health.

Resuming physical activity following COVID-19 requires individualized consideration of health status, illness severity, and guidance from healthcare professionals. Initial concerns during the pandemic suggested frequent cardiac involvement; however, subsequent evidence has demonstrated a low prevalence of cardiac complications, 82–84 making routine comprehensive pre-participation screening (PPS), including imaging, unnecessary for low-risk populations such as young, healthy athletes. In contrast, PPS is warranted in the presence of cardiac symptoms, moderate-to-severe infection, ECG anomalies, or ventricular arrhythmias to rule out cardiac sequelae, particularly myocarditis. Myocarditis is a recognized cause of sudden cardiac death (SCD) in young athletes and non-athletes.

According to current ESC guidelines on sports cardiology, <sup>86</sup> individuals diagnosed with myocarditis should refrain from all physical activity for 3–6 months, depending on the severity of the condition. RTP is only recommended following complete resolution of myocarditis without residual complications, including normalisation of LVEF, consistent with protocols for other myocarditis-causing infections. A repeat CMR using T2 imaging (preferably with T2 mapping) can indicate resolution of oedema and enable faster and safer RTP. The RTP process should be gradual and guided by cardiopulmonary exercise testing to assess exercise intensity thresholds, facilitate a safe reintroduction to physical activity, and minimize the risk of relapses.

#### Long COVID and exercise rehabilitation

Some individuals may experience Long COVID, characterized by clinical manifestations such as fatigue and exercise intolerance. These symptoms are often linked to deconditioning and reduced exercise capacity. Exercise training has shown potential benefits in aiding recovery for patients with Cardiac Long COVID.<sup>87</sup> Preliminary studies indicate that exercise rehabilitation can

improve cardiorespiratory and musculoskeletal fitness, functional status, fatigue, and quality of life in post-COVID-19 patients. Early intervention during symptomatic COVID-19 is crucial to prevent Long COVID syndrome and mitigate the chronicity of fatigue.

Exercise programmes for Long COVID patients should be personalized, considering their clinical and individual characteristics and investigations undertaken. <sup>86</sup> Close follow-up is necessary to monitor progress and adapt the exercise regimen as needed to optimize recovery outcomes.

Clinical advice

- Exercise prescription should be individualized based on symptoms, clinical presentation, and the type of physical activity (competitive vs. recreational).
- In cases of confirmed myocarditis, all recreational and competitive sports should cease for a minimum of 3 months. Resumption of activity should be permitted only when the patient is asymptomatic and free of sequelae, following medical evaluation.

### Unmet needs and future perspectives

As our understanding of COVID-19 and its cardiovascular implications continues to develop, significant knowledge gaps persist, particularly regarding the long-term cardiovascular sequelae of COVID-19, the effects of reinfections, and vaccine-related adverse events such as myocarditis. <sup>24</sup> Our treatment strategies in these areas rely on limited evidence, highlighting the urgent need for more comprehensive and longitudinal studies. The interaction between COVID-19 and pre-existing cardiovascular conditions also warrants further investigation to refine preventive measures and develop individualized treatment approaches. <sup>88</sup>

A critical area for advancement is the establishment of clearer guidelines for cardiovascular rehabilitation tailored to COVID-19 survivors, particularly those experiencing Long COVID. The roles of lifestyle modifications, pharmacological therapies, and novel diagnostic tools remain inadequately understood, emphasizing the necessity of research across diverse populations including more women and those in higher deprivation. Personalized rehabilitation strategies will be essential to improve long-term cardiovascular outcomes for these patients.<sup>89</sup>

Moving forward, international collaboration in research will be pivotal in addressing these unmet needs, enabling the development of more targeted interventions, and contributing to the reduction of the global cardiovascular burden associated with COVID-19.

# **Conclusions**

The cardiovascular implications of COVID-19, spanning acute infection, Long COVID, and vaccine-related complications, continue to present a significant public health challenge. This clinical consensus statement emphasizes the necessity of early recognition of Long COVID, a personalized approach, individualized rehabilitation, evidence-based pharmacotherapy, interventions (where available as discussed in this statement), and long-term monitoring to mitigate cardiovascular complications.

Multidisciplinary care and personalized treatment plans are fundamental to improving outcomes, while ongoing research into the long-term cardiovascular effects of COVID-19 remains crucial. Future studies must prioritize optimizing prevention and rehabilitation strategies, addressing existing knowledge gaps, and delivering evidence-based recommendations to manage the evolving cardiovascular burden of the pandemic effectively.

# Supplementary material

Supplementary material is available at European Journal of Preventive Cardiology.

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# **Author contribution**

V.S.V., V.T., and G.B.-Z. conceived and designed the study. All authors contributed to with writing part of the document. V.S.V. drafted the final version. All authors reviewed and approved the final manuscript.

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# **Data availability**

None declared.

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